IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	: Adam S. Cantor et al.	Art Unit	: 1615
Serial No.	: 09/965,610	Examiner	: Isis A. D. Ghali
Filed	: September 26, 2001	Conf. No.	: 8132
Title	: COMPOSITION FOR TRANSDERMAL DELIVERY OF FENTANYL		

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Commissioner for Patents
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BRIEF ON APPEAL

This brief is being filed in support of the Notice of Appeal that was filed on May 10, 2010.

(1) Real Party in Interest

The real parties in interest are 3M Company and 3M Innovative Properties Company.

(2) Related Appeals and Interferences

None.

(3) Status of Claims

Claims 1-9, 16-18, 28-29, 35-36, and 39-103 are pending. Claims 48-51 and 55-91 have been withdrawn. Claims 1-5, 35, 39-42, 52-53, and 91-97 stand rejected under 35 USC § 102(b) over Miranda et al., US 5,474,783 ("Miranda"). Claims 1-9, 16-18, 28-29, 35-36, 39-47, 52-54, and 92-103 stand rejected under 35 USC § 103 over Miranda in view of Garbe et al., WO 96/08229 ("Garbe").

(4) Status of Amendments

All amendments have been entered.

(5) Summary of Claimed Subject Matter

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Claims 1-9, 16-18, 28-29, 35-36, 39-47, 52-54, and 92-103 are directed towards a transdermal drug delivery composition consisting essentially of: (a) a copolymer comprising (i) one or more A monomers selected from the group consisting of alkyl acrylates containing 4 to 12 carbon atoms in the alkyl group and alkyl methacrylates containing 4 to 12 carbon atoms in the alkyl group; and (ii) one or more ethylenically unsaturated B monomers copolymerizable with the A monomer; (b) about 8% to about 30% by weight fentanyl based on the total weight of the composition; and, optionally, (c) a component selected from the group consisting of delivery enhancing adjuvants, tackifiers, plasticizers, and combinations thereof. Specification, p. 1/[0017]-[0025]; p. 2/[0036]-[0037]. The composition is free of undissolved fentanyl. Specification, p. 2, [0036].

(6) Grounds of Rejection to be Reviewed on Appeal

A. Does Miranda anticipate claims 1-5, 35, 39-42, 52-53 and 91-97?

B. Does the proposed combination of Miranda and Garbe render obvious claims 1-9, 16-18, 28-29, 35-36, 39-47, 52-54, and 92-103?

(7) Argument

A. Miranda does not anticipate claims 1-5, 35, 39-42, 52-53, and 91-97 because the claims exclude Miranda's polysiloxane

Claims 1-5, 35, 39-42, 52-53, and 91-97 are directed towards transdermal drug delivery compositions for delivering fentanyl "consisting essentially of" an acrylate copolymer, fentanyl, and, in some cases, certain specified ingredients (adjuvants, plasticizers, and tackifiers). The claims stand rejected as anticipated by Miranda. Miranda describes transdermal drug delivery compositions that **require** at least two polymers having different solubility parameters. In one embodiment, one of the polymers is a polyacrylate adhesive and the other is a polysiloxane adhesive. Miranda criticizes compositions that include only a single adhesive polymer (e.g., col. 2, lines 4-16), and states that the second adhesive polymer modulates the release of the drug from the adhesive composition (col. 6, lines 16-19 and col. 8, lines 30-43) (emphasis added):

> The invention is **premised** on the discovery that the transdermal permeation rate of a drug from the multiple adhesive system can be selectively

> modulated by adjusting the solubility of the drug in the device …. In a particularly preferred embodiment of the invention, the multiple polymer adhesive comprises a blend of an acrylic pressure-sensitive adhesive and a silicone pressure-sensitive adhesive …. **The amount of acrylic-based polymer (hereinafter referred to broadly as a polyacrylate) and silicone-based polymer (hereinafter referred to broadly as a polysiloxane) is selected to modify the saturation concentration of the drug in the multiple polymer adhesive system in order to affect the rate of delivery of the drug from the system and through the skin.**

Miranda, therefore, clearly teaches adding an amount of polysiloxane to the polyacrylate that is specifically designed to affect the transdermal drug delivery properties of the composition.

As the Examiner correctly notes on pp. 10-11 of the Office Action mailed 3/25/10, "'consisting essentially of' limits the scope of the claim to the specified ingredients, and those that do not materially affect the basic and novel characteristics of the composition." In this case, the listed ingredients are an acrylate copolymer, fentanyl, and, in some cases, certain specified ingredients (adjuvants, plasticizers, and tackifiers). The "basic and novel characteristics" of this composition relate to the transdermal delivery of fentanyl. Accordingly, the issue with respect to Miranda is whether the "consisting essentially of" language in the claims excludes Miranda's polysiloxanes. Resolution of this issue turns on whether inclusion of Miranda's polysiloxanes would affect the transdermal drug delivery properties of the claimed compositions. An ingredient may "affect" the transdermal drug delivery properties of the composition either positively or negatively. The "consisting essentially of" language does not merely exclude ingredients that detrimentally affect the transdermal drug delivery properties of the composition.

The Examiner's position is that the "consisting essentially of" language in Appellants' claims does not exclude Miranda's polysiloxanes, presumably because there is no evidence that inclusion of the polysiloxanes detrimentally affects the properties of the claimed transdermal drug delivery compositions. The Examiner states (p. 11):

> [A]pplicant has the burden of showing the basic and novel characteristics of the claimed composition, i.e. showing that the introduction of these components would materially change the characteristics of applicant's composition …. Applicants disclosed in their specification, page 7, lines 20-25, that polysiloxanes are suitable pressure sensitive adhesive for their invention. Nothing of record shows that polysiloxanes have detrimental effect on the acrylate polymer of the invention.

Miranda itself belies the Examiner's position. The entire reason Miranda includes the polysiloxanes is to affect the drug delivery characteristics of the composition. As is evident from the passage quoted above, Miranda specifically instructs selecting the amount of polysiloxane to achieve this very purpose. It is irrelevant that there is no evidence of record showing that Miranda's polysiloxanes would have a detrimental effect on Appellants' acrylate copolymer. "Detrimental effect" is not the standard. It is equally irrelevant that Appellants' specification discloses polysiloxanes because merely listing them says nothing about whether they affect the transdermal drug delivery characteristics of an acrylate-containing composition. The only evidence of record on the issue of whether Miranda's polysiloxanes would affect the drug delivery properties of an acrylate-containing transdermal drug delivery composition is what Miranda says—and Miranda makes absolutely clear that the polysiloxanes, when added in the amounts Miranda instructs, do, in fact, affect the transdermal drug delivery properties of the composition. The Examiner has produced no evidence to the contrary. The "consisting essentially of " language included in each of Appellants' claims, therefore, plainly excludes Miranda's polysiloxanes because, based upon what Miranda itself discloses, the additional presence of such polysiloxanes would affect the drug delivery characteristics of Appellants' acrylate copolymer-based, transdermal drug delivery compositions. Accordingly, Miranda cannot anticipate the claims. The rejections, therefore, should be reversed.

B. The proposed combination of Miranda and Garbe does not render claims 1-9, 16-18, 28-29, 35-36, 39-47, 52-54, and 92-103 obvious

The Examiner's proposed combination of Miranda and Garbe for obviousness purposes is improper. The rejection is based upon the premise that because Garbe describes acrylate polymers without polysiloxanes, it would have been obvious to combine the teachings of the two references, while at the same time omitting Miranda's polysiloxanes (p.11):

> Garbe teaches that acrylates can be used without polysiloxanes adhesives. The copolymer instantly claimed was known in the art at the time of the invention. Further, it has been held that omission of an element and its function is obvious if the function of the element is not desired.

The Examiner's proposed combination ignores the fact that Miranda expressly teaches that the presence of the polysiloxane is critical. In fact, in Miranda's own words, Miranda's invention is "premised" on including more than one polymer in the drug delivery composition for the purpose of affecting transdermal drug delivery. In Miranda's compositions, the function of the polysiloxane is absolutely desired and necessary. In this regard, it is irrelevant that Garbe's compositions lack the polysiloxane because one cannot use the absence of polysiloxanes in Garbe's composition as a license to ignore Miranda's plain admonition that a transdermal drug delivery-altering amount of polysiloxane must be included. On the contrary, what it means is that the two references simply cannot be combined—or, at the very least, cannot be combined to yield a composition that lacks Miranda's polysiloxanes, which Appellants' claims exclude. *See Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc.*, 796 F.2d 443, 448, 230 USPQ 416, 419 (Fed. Cir. 1986), quoting *In re Wesslau*, 353 F.2d 238, 241, 147 USPQ 391, 393 (CCPA 1965):

> It is impermissible within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one skilled in the art.

For at least the reasons discussed above, the pending claims are patentable over the proposed combination of Miranda and Garbe. Accordingly, rejections should be reversed.

The brief fee of $540 is enclosed. Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

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Appendix of Claims

1. A transdermal drug delivery composition consisting essentially of:

(a) a copolymer comprising

(i) one or more A monomers selected from the group consisting of alkyl acrylates containing 4 to 12 carbon atoms in the alkyl group and alkyl methacrylates containing 4 to 12 carbon atoms in the alkyl group; and

(ii) one or more ethylenically unsaturated B monomers copolymerizable with the A monomer; and

(b) about 8% to about 30% by weight fentanyl based on the total weight of the composition; and, optionally,

(c) a component selected from the group consisting of delivery enhancing adjuvants, tackifiers, plasticizers, and combinations thereof,

wherein the composition is free of undissolved fentanyl.

2. The composition of claim 1 wherein the A monomer is selected from the group consisting of isooctyl acrylate, 2-ethylhexyl acrylate, butyl acrylate, and cyclohexyl acrylate.

3. The composition of claim 1 wherein the A monomer is isooctyl acrylate.

4. The composition of claim 1 wherein the B monomer is selected from the group consisting of 2-hydroxyethyl acrylate, 2-hydroxyethyl methacrylate, glyceryl acrylate, N,N-diethylacrylamide, 2-ethoxyethoxyethyl acrylate, 2-ethoxyethyl acrylate, tetrahydrofurfuryl acrylate, acrylic acid, acrylamide, vinyl acetate, N-vinyl pyrrolidone and mixtures thereof.

5. The composition of claim 1 wherein the B monomer is 2-hydroxyethyl acrylate.

6. The composition of claim 5 wherein the copolymer comprises from about 5% to about 45% of 2-hydroxyethyl acrylate by weight based on the total weight of all monomers in the copolymer.

7. The composition of claim 1 wherein the copolymer further comprises a macromonomer.

8. The composition of claim 7 wherein the macromonomer is a functionally terminated polymethylmethacrylate.

9. The composition of claim 7 wherein the copolymer contains from about 1% to about 6% of macromonomer by weight based on the total weight of all monomers in the copolymer.

16. The composition of claim 1 wherein the concentration of fentanyl in said transdermal drug delivery composition is from about 12% to about 24% by weight.

17. The composition of claim 7 wherein the copolymer comprises from about 50 to about 94% isooctyl acrylate, about 5% to about 40% 2-hydroxyethyl acrylate, about 1% to about 6% macromonomer, and 0% to about 20% vinyl acetate by weight.

18. The composition of claim 7 wherein the copolymer comprises from about 52% to about 60% isooctyl acrylate, about 35% to about 40% 2-hydroxyethyl acrylate, about 1% to about 4% macromonomer, and 0% to about 10% vinyl acetate by weight.

28. A method of treating in a mammal a condition capable of treatment by fentanyl comprising the steps of:

(a) providing a composition according to claim 1;

(b) placing the composition on the skin of a mammal; and

(c) allowing the composition to remain on the skin for a time sufficient to establish or maintain a therapeutically effective blood level of fentanyl in the mammal.

29. A method of providing analgesia to a mammal comprising the steps of:

(a) providing a composition according to claim 1;

(b) placing the composition on the skin of a mammal; and

(c) placing the composition to remain on the skin for a time sufficient to establish or maintain an analgesically effective blood level of fentanyl in the mammal.

35. A transdermal drug delivery composition consisting essentially of:

(a) a copolymer comprising:

(i) one or more A monomers selected from the group consisting of isooctyl acrylate, 2-ethylhexyl acrylate, butyl acrylate, and cyclohexyl acrylate; and

(ii) one or more ethylenically unsaturated B monomers copolymerizable with the A monomer; wherein the B monomers are selected from the group consisting of 2-hydroxyethyl acrylate, 2-hydroxyethyl methacrylate, glyceryl acrylate, N,N-diethylacrylamide, 2-ethoxyethoxyethyl acrylate, 2-ethoxyethyl acrylate, tetrahydrofurfuryl acrylate, acrylic acid, acrylamide, vinyl acetate, N-vinyl pyrrolidone and mixtures thereof; and

(b) about 8% to about 30% by weight fentanyl based on the total weight of the composition; and, optionally,

(c) a component selected from the group consisting of delivery enhancing adjuvants, tackifiers, plasticizers, and combinations thereof,

wherein the composition is free of undissolved fentanyl.

36. A transdermal drug delivery composition consisting essentially of:

(a) a copolymer comprising:

(i) one or more A monomers selected from the group consisting of isooctyl acrylate, 2-ethylhexyl acrylate, butyl acrylate, and cyclohexyl acrylate; and

(ii) about 5% to about 45% of one or more ethylenically unsaturated B monomers copolymerizable with the A monomer; wherein the B monomers are selected from the group consisting of 2-hydroxyethyl acrylate, 2-hydroxyethyl methacrylate, glyceryl acrylate, N,N-diethylacrylamide, 2-ethoxyethoxyethyl acrylate, 2-ethoxyethyl acrylate, tetrahydrofurfuryl acrylate, acrylic acid, acrylamide, vinyl acetate, N-vinyl pyrrolidone and mixtures thereof; and

(b) about 8% to about 30% by weight fentanyl based on the total weight of the composition; and, optionally,

(c) a component selected from the group consisting of delivery enhancing adjuvants, tackifiers, plasticizers, and combinations thereof,

wherein the composition is free of undissolved fentanyl.

39. The composition of claim 1 wherein the composition contains a delivery enhancing adjuvant.

40. The composition of claim 39 wherein the delivery enhancing adjuvant is selected from the group consisting of alkane polyols, fatty acids, fatty acid esters, fatty alcohols, terpenes, C_5-C_{18} alkyl esters of a carboxylic acid, and mixtures thereof.

41. The composition of claim 39 wherein the delivery enhancing adjuvant is selected from the group consisting of ethyl oleate, isopropyl myristate, glycerol, tetraglycol, methyl laurate, N,N-dimethyldodecylamine N-oxide, limonene, terpineol, tetraethylene glycol, menthol, and mixtures thereof.

42. The composition of claim 39 wherein the concentration of the delivery enhancing adjuvant is from about 5% to about 40% by weight based on the total weight of the composition.

43. The composition of claim 39 wherein the delivery enhancing adjuvant is tetraglycol.

44. The composition of claim 39 wherein the delivery enhancing adjuvant is methyl laurate.

45. The composition of claim 17 wherein the concentration of fentanyl is from about 12% to about 22% by weight, and wherein the composition contains about 15% to about 35% by weight of a delivery enhancing adjuvant selected from the group consisting of methyl laurate, tetraglycol, and mixtures thereof.

46. The composition of claim 45 wherein the concentration of fentanyl is from about 12% to about 17% by weight and the concentration of methyl laurate is from about 20% to about 35% by weight.

47. The composition of claim 45 wherein the concentration of fentanyl is from about 15% to about 22% by weight and the concentration of tetraglycol is from about 15% to about 25% by weight.

52. A device for the transdermal delivery of fentanyl comprising a backing and a composition according to claim 1, said composition being adhered to one surface of the backing.

53. The composition of claim 39 wherein the delivery enhancing adjuvant is a skin permeation enhancer.

54. A transdermal drug delivery composition consisting essentially of:

(a) a copolymer comprising

(i) one or more A monomers selected from the group consisting of isooctyl acrylate, 2-ethylhexyl acrylate, butyl acrylate, and cyclohexyl acrylate; and

(ii) about 5% to about 45% of one or more ethylenically unsaturated B monomers copolymerizable with the A monomer; wherein at least one B monomer is 2-hydroxyethyl acrylate; and

(b) about 8% to about 30% by weight fentanyl based on the total weight of the composition; and

(c) a delivery enhancing adjuvant selected from the group consisting of methyl laurate, tetraglycol, and mixtures thereof;

wherein the composition is substantially free of undissolved fentanyl.

92. A transdermal drug delivery composition consisting essentially of:

(a) a copolymer comprising

(i) one or more A monomers selected from the group consisting of alkyl acrylates containing 4 to 12 carbon atoms in the alkyl group and alkyl methacrylates containing 4 to 12 carbon atoms in the alkyl group; and

(ii) one or more ethylenically unsaturated B monomers copolymerizable with the A monomer; and

(b) about 8% to about 30% by weight fentanyl based on the total weight of the composition;

wherein the composition is free of undissolved fentanyl.

93. A device according to claim 92, wherein the concentration of fentanyl in said composition is about 8% by weight.

94. A device for the transdermal delivery of fentanyl comprising a backing and a composition according to claim 92, said composition being adhered to one surface of the backing.

95. A transdermal drug delivery composition consisting essentially of:

(a) a copolymer of:

(i) one or more A monomers selected from the group consisting of isooctyl acrylate, 2-ethylhexyl acrylate, butyl acrylate, and cyclohexylacrylate; and

(ii) one or more ethylenically unsaturated B monomers copolymerizable with the A monomer, wherein the B monomers are selected from the group consisting of 2-hydroxyethyl acrylate, 2-hydroxymethacrylate, vinyl acetate, glycidyl methacrylate, and mixtures thereof; and

(b) about 8% to about 30% by weight fentanyl based on the total weight of the composition;

wherein the composition is free of undissolved fentanyl.

96. A composition according to claim 95, wherein the concentration of fentanyl in said composition is about 8% by weight.

97. A device for the transdermal delivery of fentanyl comprising a backing and a composition according to claim 95, said composition being adhered to one surface of the backing.

98. A transdermal drug delivery composition consisting essentially of:

(a) a copolymer comprising

(i) about 40 to about 95% by weight of one or more A monomers selected from the group consisting of alkyl acrylates containing 4 to 12 carbon atoms in the alkyl group and alkyl methacrylates containing 4 to 12 carbon atoms in the alkyl group;

(ii) about 5 to about 55% by weight of one or more ethylenically unsaturated B monomers copolymerizable with the A monomer; and

(iii) 0 to about 20% by weight of one or more macromonomers copolymerizable with the A and B monomers;

(b) about 8% to about 30% by weight fentanyl based on the total weight of the composition; and, optionally,

(c) a component selected from the group consisting of delivery enhancing adjuvants, tackifiers, plasticizers, and combinations thereof,

wherein the composition is free of undissolved fentanyl.

99. A composition according to claim 98, wherein the concentration of fentanyl in said composition is about 8% by weight.

100. A composition according to claim 98, wherein the copolymer contains from about 1% to about 6% of the macromonomer by weight based on the total weight of all monomers in the copolymer.

101. A composition according to claim 98, wherein the composition includes a delivery enhancing adjuvant.

102. A composition according to claim 101, wherein the delivery enhancing adjuvant is selected from the group consisting of methyl laurate, isopropyl myristate, and mixtures thereof.

103. A device for the transdermal delivery of fentanyl comprising a backing and a composition according to claim 98, said composition being adhered to one surface of the backing.

Evidence Appendix

None.

Related Proceedings Appendix

None.